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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 1 of 15

Complete if Known

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 1015 / 623
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>MC</i>	1	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39:4569-4575	
	2	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29(4):483-486	
	3	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Cancer Metast. Rev.</i> (1995) 14:59-73	
	4	ANDERSEN et al. "Detection of C-ERBB-2 related protein in sera from breast cancer patients" <i>Acta Oncol.</i> (1995) 34(4):499-504	
	5	ANGLADA et al. "N,N'-cyclization of carbodiimides with 2-(bromomethyl)acrylic acid. A direct entry to the system 5-methylene-6H-pyrimidine-2,4-dione, A new class of thymine analogues" <i>J. Heterocyclic Chem.</i> (July-Aug. 1996) 33:1259-1270	
	6	ANTELMAN et al. "Inhibition of tumor cell proliferation in vitro and in vivo by exogenous p110 ^{KB} , the retinoblastoma tumor suppressor protein" <i>Oncogene</i> (1995) 10:697-704	
	7	ASAKURA and ROBINS, "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" <i>Tetrahedron Lett.</i> (1988) 29(23):2855-2858	
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	9	AZISI et al. "Comparison of the antiviral effects of 5-methoxymethyldeoxyuridine-5'-monophosphate with adenine arabinoside-5'-monophosphate" <i>Antivir. Res.</i> (1983) 3:161-174	
	10	BAGSHAWE "Antibody-directed enzyme prodrug therapy: A review", <i>Drug Develop. Res.</i> (1995) 34(2):220-230	
	11	BAJETTA et al. "A pilot safety study of capecitabine, a new oral fluoropyrimidine, in patients with advanced neoplastic disease" <i>Tumori</i> (1996) 82:450-452	
	12	BALZARINI et al. "Incorporation of 5-substituted pyrimidine nucleoside analogues into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line" <i>Meth. Find. Exp. Clin. Pharmacol.</i> (1985) 7(1):19-28	
<i>MC</i>	13	BALZARINI et al. "Thymidylate synthase is the principal target enzyme for the cytostatic activity of (E)-5-(2-bromovinyl)-2'-deoxyuridine against murine mammary carcinoma (FM3A) cells transformed with the herpes simplex virus type 1 or type 2 thymidine kinase gene" <i>Mol. Pharmacol.</i> (1987) 32:410-416	

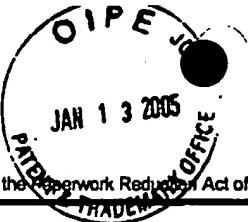
Examiner's Signature	L. E. Crane <i>L. E. Crane</i>	Date Considered	09/21/2005
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Sheet 2 of 15

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<i>Jee</i>	14	BALZARINI et al. "Differential mechanism of cytostatic effect of (E)-5-(2-bromovinyl)-2'-deoxyuridine, 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antiherpetic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" <i>J. Biol. Chem.</i> (1993) 268(9):6332-6337	
	15	BALZARINI et al. "Anti-HIV and anti-HBV activity and resistance profile of 2',3'-dideoxy-3'-thiacytidine (3TC) and its arylphosphoramidate derivative CF 1109" <i>Biochem. Biophys. Res. Co.</i> (1996) 225:363-369	
	16	BALZARINI et al. "Conversion of 2',3'-dideoxyadenosine (ddA) and 2',3'-didehydro-2',3'-dideoxyadenosine (d4A) to their corresponding aryloxyphosphoramidate derivatives markedly potentiates their activity against human immunodeficiency virus and hepatitis B virus" <i>FEBS Lett.</i> (1997) 410:324-328	
	17	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochim. Pol.</i> (1995) 42(4):457-464	
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	19	BARBATO, et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4,3-c] pyrimidine nucleoside analogues" <i>Nucleos. Nucleot.</i> (1991) 10(4):853-866	
	20	BARBOUR et al. "A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxyuridine in mammalian and bacterial cells" <i>Mol. Pharmacol.</i> (1992) 42:242-248	
	21	BARR "Inhibition of thymidylate synthetase by 5-alkynyl-2'-deoxyuridylates" <i>J. Med. Chem.</i> (1981) 24(12):1385-1388	
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	23	BARR et al. "Reaction of 5-ethynyl-2'-deoxyuridylate with thiols and thymidylate synthetase" <i>Biochemistry</i> (1983) 22:1696-1703	
	24	BARRETT "Trapping of the C5 methylene intermediate in thymidylate synthase" <i>J. Am. Chem. Soc.</i> (1998) 120:449-450	
<i>Jee</i>	25	BENZARIA et al. "Synthesis, <i>in vitro</i> antiviral evaluation, and stability studies of bis(S-acyl-2-thioethyl) ester derivatives of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA) as potential PMEA prodrugs with improved oral bioavailability" <i>J. Med. Chem.</i> (1996) 39:4958-4965	

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Art Unit	1623 --1615--
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<i>He</i>	26	BERGSTROM et al. "C-5-substituted pyrimidine nucleosides. 3. Reaction of allylic chlorides, alcohols, and acetates with pyrimidine nucleoside derived organopalladium intermediates" <i>J. Org. Chem.</i> (1981) 46(7):1432-1441	
<i>He</i>	27	BERGSTROM et al. "Synthesis of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine and related analogues: Potent and unusually selective antiviral activity of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine against herpes simplex virus type 1" <i>J. Med. Chem.</i> (1984) 27:279-284	
<i>He</i>	28	BERKOW et al. (eds). <i>The Merck Manual of Diagnosis and Therapy</i> , 16th Edition, Merck & Co., Rahway, NJ, (May 1992) only page 1278 supplied	
<i>He</i>	29	BERTINO et al. "Resistance mechanisms to methotrexate in tumors" <i>Stem Cells</i> (1996) 14:5-9	
	30	BIGGE et al. "Palladium-catalyzed coupling reactions of uracil nucleosides and nucleotides" <i>J. Amer. Chem. Soc.</i> (Mar. 12, 1980) 102(6):2033-2038	
	31	BLACKLEDGE "New developments in cancer treatment with the novel thymidylate synthase inhibitor raltitrexed ('Tomudex')" <i>British J. Cancer</i> (1998) 77(Supp 2):29-37	
	32	BOSSLET et al. "A novel one-step tumor-selective prodrug activation system" <i>Tumor Targeting</i> (1995) 1:45-50	
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<i>He</i>	40	CHAUDHURI and KOOL "Very high affinity DNA recognition by bicyclic and cross-linked oligonucleotides" <i>J. Am. Chem. Soc.</i> (1995) 117:10434-10442	

Examiner's Signature

L. E. Crane

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Sheet

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Examiner Name	Not Yet Assigned

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	41	CHEN et al. "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Cancer Res.</i> (Mar. 15, 1996) 56:1331-1340	
	42	CHO and JOHNSON "(E)-5-(3-oxopropen-1-yl)-2'-deoxyuridine and (E)-5-(3-oxopropen-1-yl)-2',3'-dideoxyuridine; New antiviral agents: Synthesis and biological activity" <i>Tetrahedron Lett.</i> (1994) 35(8):1149-1152	
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***	52	DAGLE et al. "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: Studies of An2 and Cyclin in embryogenesis" <i>Nucleic Acids Res.</i> (Aug. 25, 1990) 18(16):4751-4757	
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	56	DeCLERCQ et al. "Nucleic acid related compounds. 40. Synthesis and biological activities of 5-alkynyluracil nucleosides" <i>J. Med. Chem.</i> (1983) 26:661-666	
	57	DICKER et al. "Methotrexate resistance in an <i>in vivo</i> mouse tumor due to a non-active-site dihydrofolate reductase mutation" <i>PNAS USA</i> (Dec. 1993) 90:11797-11801	
	58	DIRVIN et al. "The role of human glutathione S-transferase isoenzymes in the formation of glutathione conjugates of the alkylating cytostatic drug thiotepa" <i>Cancer Res.</i> (April 15, 1995) 55:1701-1706	
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	60	DUNN, III et al. "Solution of the conformation and alignment tensors for the binding of trimethoprim and its analogs to dihydrofolate reductase: 3D-quantitative structure-activity relationship study using molecular shape analysis, 3-way partial least-squares regression, and 3-way factor analysis" <i>J. Med. Chem.</i> (1996) 39:4825-4832	
	61	DYER et al. "Nucleic Acids Chemistry: Improved and new synthetic procedures, methods, and techniques" Townsend, L. B. & Tipson, R. S., eds. (Wiley-Interscience, New York, NY) (1991) 4:79-83	
	62	ECCLES et al. "Significance of the c-erbB family of receptor tyrosine kinases in metastatic cancer and their potential as targets for immunotherapy" <i>Invasion Metastasis</i> (1994-95) 14(1-6):337-348	
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**	64	EVARD et al. "An <i>in vitro</i> nucleoside analog screening method for cancer gene therapy" <i>Cell Biol. Toxicol.</i> (1996) 12:345-350	
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	66	FARQUHAR et al. "Synthesis and antitumor evaluation of bis[(pivaloyloxy)methyl] 2'-deoxy-5-fluorouridine 5'-monophosphate (FdUMP): A strategy to introduce nucleotides into cells" <i>J. Med. Chem.</i> (1994) 37:3902-3909	
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	70	FINCH "Radiation Injury" In: <i>Harrison's Principles of Internal Medicine</i> , 12th Edition, McGraw-Hill, Inc., New York, NY (1991) 2204-2208	

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	71	FINER-MOORE et al. "Refined structures of substrate-bound and phosphate-bound thymidylate synthase from <i>Lactobacillus casei</i> " <i>J. Mol. Biol.</i> (1993) 232:1101-1116	
	72	FINER-MOORE et al. "Crystal structure of thymidylate synthase from T4 phage: Component of a deoxyribonucleoside triphosphate-synthesizing complex" <i>Biochemistry</i> (1994) 33:15459-15468	
***	73	FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>J. Invest. Dermatol.</i> (May 1990) 94(5):657-661	
	74	FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>Chem Abstracts</i> (1990) 113:Abstract No. 254	
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Examiner's Signature	L. E. Crane	Date Considered	09/21/2005
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Complete if Known

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>JEC</i>	87	HANDFIELD and LEVESQUE "Strategies for isolation of in vitro expressed genes from bacteria" <i>FEMS Microbiol. Revs.</i> (1999) 23:69-91	
**	88	HAKIMELAHI et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" <i>J. Med. Chem.</i> (Nov. 10, 1995) 38(23):4648-4659	
<i>JEC</i>	89	HARDY et al. "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> (Jan. 23, 1987) 235:448-455	
	90	HARRIS et al. "Adenovirus-mediated p53 gene transfer inhibits growth of human tumor cells expressing mutant p53 protein" <i>Cancer Gene Ther.</i> (1996) 3(2):121-130	
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<i>JEC</i>	99	HSAIO and BARDOSE "Synthesis of 5'-thymidinyl bis(1-aziridinyl)phosphinates as antineoplastic agents" <i>J. Med. Chem.</i> (1981) 24:887-889	

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 -1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

NON PATENT LITERATURE DOCUMENTS

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	100	HU et al. "Determination of absorption characteristics of AG337, a novel thymidylate synthase inhibitor, using a perfused rat intestinal model" <i>J. Pharmaceutical Sciences</i> (July 1998) 87(7):886-890	
	101	HUANG and SANTI "Active site general catalysts are not necessary for some proton transfer reactions of thymidylate synthase" <i>Biochemistry</i> (1997) 36:1869-1873	
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E. Crane

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

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Complete if Known

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit.	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published
	115	KODAMA et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> (1996) 40(5):359-363
	116	KUMAR et al. "Synthesis and biological evaluation of some cyclic phosphoramidate nucleoside derivatives" <i>J. Med. Chem.</i> (Sept. 1990) 33(9):2368-2374
	117	KUNDU et al. "Synthesis and biological activities of [E]-5-(2-acrylvinyl) uracils" <i>Eur. J. Med. Chem.</i> (1993) 28:473-479
	118	KUROBOSHI and HIYAMA "A facile synthesis of difluoromethylene compounds by oxidative fluorodesulfurization of dithioacetals using tetrabutylammonium dihydrogentrifluoride and N-halo compounds" <i>SYNLETT</i> (Dec. 1991) pp. 909-910
	119	KUROBOSHI and HIYAMA "A facile synthesis of α,α -difluoroalkyl ethers and carbonyl fluoride acetals by oxidative desulfurization-fluorination" <i>SYNLETT</i> (April 1994) pp. 251-252
	120	LAM "Application of combinatorial library methods in cancer research and drug discovery" <i>Anti-Cancer Drug Design</i> (1997) 12:145-167
	121	LARSSON et al. "Thymidylate synthase in advanced gastrointestinal and breast cancers" <i>Acta Oncologica</i> (1996) 35(4):469-472
	122	LASIC "Doxorubicin in sterically stabilized liposomes" <i>Nature</i> (Apr. 11, 1996) 380:561-562
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	125	LIN et al., "Rhenium188 hydroxyethylidene diphosphonate: a new generator-produced radiotherapeutic drug of potential value for the treatment of bone metastases" <i>Eur. J. Nucl. Med.</i> 24(6):590-595 (June 1997)
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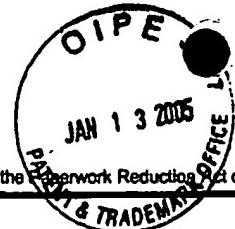
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First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned

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	130	MASTERS and ALTARDI "The nucleotide sequence of the cDNA coding for the human dihydrofolic acid reductase" <i>Gene</i> (1983) 21:59-63	
	131	McGUIGAN et al. "Certain phosphoramidate derivatives of dideoxy uridine (ddU) are active against HIV and successfully by-pass thymidine kinase" <i>FEBS Lett</i> (1994) 351:11-14	
	132	McGUIGAN "Aryl phosphate derivatives of AZT retain activity against HIV1 in cell lines which are resistant to the action of AZT" <i>Antivir. Res.</i> (1992) 17:311-321	
	133	McGUIGAN "Intracellular delivery of bioactive AZT nucleotides by aryl phosphate derivatives of AZT" <i>J. Med. Chem.</i> (1993) 36:1048-1052	
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	135	McGUIGAN et al. "Synthesis and evaluation of some masked phosphate esters of the anti-herpetic drug 882C (netividine) as potential antiviral agents" <i>Antivir. Chem. Chemoth.</i> (1998) 9:233-243	
	136	McINTEE "Probing the mechanism of action and decomposition of amino acid phosphomonoester amides of antiviral nucleoside prodrugs" <i>J. Med. Chem.</i> (1997) 40:3323-3331	
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	140	MEIER et al. "ADA-bypass by lipophilic cyclosal-ddAMP pro-nucleotides a second example of the efficiency of the cyclosal-concept" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(12):1577-1582	
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Examiner's Signature

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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JEC	146	MONTFORT and WEICHSEL "Thymidylate synthase: Structure, inhibition, and strained conformations during catalysis" <i>Pharmacol. Ther.</i> (1997) 76(1-3):29-43	
	147	MONTGOMERY et al., "Phosphonate analogue of 2'-deoxy-5-fluorouridylic acid" <i>J. Med. Chem.</i> (1979) 22(1):109-111	
JEC	148	MORGAN et.al. "Tumor efficacy and bone marrow-sparing properties of TER286, a cytotoxin activated by glutathione S-transferase" <i>Cancer Res.</i> (June 15, 1998) 58:2568-2575	
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JEC	150	MURAKAMI and SEKIYA "Accumulation of genetic alterations and their significance in each primary human cancer and cell line" <i>Mutat. Res.</i> (1998) 400(1-2):421-437	
**	151	NAESENS et.al. "Anti-HIV-activity-and-metabolism-of-phosphoramidate derivatives of D4T-MP with Variations in the amino acid moiety" Poster Session 1, <i>The Tenth International Conference on Antiviral Research</i> , Hotel Nikko, Atlanta, GA April 6-11, 1997; published in <i>Antivir. Research</i> (April 1997) 34(2):A54 (Abstract 40)	
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	153	NICHOL and HAKALA "Comparative growth-inhibitory activity of homofolic acid against cell lines sensitive and resistant to amethopterin" <i>Biochem. Pharmacol.</i> (Oct. 1966) 15(10):1621-1623	
	154	NOOTER and STOTER "Molecular mechanisms of multidrug resistance in cancer chemotherapy" <i>Path. Res. Pract.</i> (1996) 192:768-780	
	155	OSAKI et al. "5-fluorouracil (5-FU) induced apoptosis in gastric cancer cell lines: Role of the p53 gene" <i>Apoptosis</i> (1997) 2:221-226	
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	157	PARDO et al. "The incorporation of deoxyuridine monophosphate in DNA increases the sister-chromatid exchange yield" <i>Exp Cell Res.</i> (1987) 168:507-517	
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Examiner's Signature	L. E. Crane	Date Considered	09/21/2005
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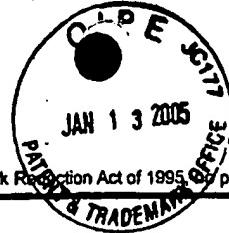
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Sheet

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of

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Complete if Known

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 - 1615 --
Examiner Name	Not Yet Assigned

Attorney Docket Number

NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	161	PETERS et al. "Thymidylate synthase and drug resistance" <i>Eur. J. Can.</i> (1995) 31A(7/8):1299-1305	
	162	PHELPS et al. "Synthesis and biological activity of 5-fluoro-2'-deoxyuridine 5'-phosphorodiamidates" <i>J. Med. Chem.</i> (1980) 23:1229-1232	
	163	PUPA et al. "The extracellular domain of the c-erbB-2 oncprotein is released from tumor cells by proteolytic cleavage" <i>Oncogene</i> (1993) 8:2917-2923	
	164	ROBERTS "An isotopic assay for thymidylate synthetase" <i>Biochemistry</i> (Nov. 1966) 5(11):3546-3548	
	165	ROBINS and BARR "Nucleic acid related compounds. 31. Smooth and efficient palladium-copper catalyzed coupling of terminal alkynes with 5-iodouracil nucleosides" <i>Tetrahedron Lett.</i> (1981) 22:421-424	
	166	ROBINS et al. "Nucleic acid related compounds. 38. Smooth and high-yield iodination and chlorination at C-5 of uracil bases and p-tolyl-protected nucleosides" <i>Can. J. Chem.</i> (1982) 60:554-557	
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	170	RONINSON et al. "Amplification of specific DNA sequences correlates with multi-drug resistance in Chinese hamster cells" <i>Nature</i> (June 14, 1984) 309:626-628	
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Examiner's Signature	E. E. Crane	Date Considered	09/21/2005
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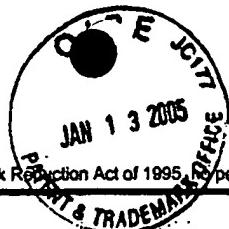
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Sheet 13 of 15

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned

Attorney Docket Number NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>Hee</i>	176	SCHIFFER et al. "Crystal structure of human thymidylate synthase: A structural mechanism for guiding substrates into the active site" <i>Biochemistry</i> (1995) 34:16279-16287	
	177	SCHIMKE "Gene amplification in cultured cells" <i>J. Biol. Chem.</i> (May 5, 1988) 263(13):5989-5992	
	178	SCHULTZ et al. "Role of thymidylate synthase in the antitumor activity of the multitargeted antifolate, LY231514" <i>Anticancer Res.</i> (1999) 19:437-444	
	179	SEGOVIA "Leishmania gene amplification: A mechanism of drug resistance" <i>Ann. Trop. Med. Parasit.</i> (1994) 88(2):123-130	
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	181	SIMON and SCHINDLER "Cell biological mechanisms of multidrug resistance in tumors" <i>PNAS USA</i> (April 1994) 91:3497-3504	
	182	SINGH et al. "Studies on the preparation and isomeric composition of ¹⁸⁶ Re- and ¹⁸⁸ Re-pentavalent rhenium dimercaptosuccinic acid complex" <i>Nucl. Med. Commun.</i> (1993) 14:197-203	
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	190	STÜHLINGER et al. "Clinical therapy and HER-2 oncogene amplification in breast cancer: Chemo vs radiotherapy" <i>J. Steroid Biochem. Molec. Biol.</i> (1994) 49(1):39-42	
<i>Hee</i>	191	SUGARMAN et al. "Recombinant human tumor necrosis factor-α: Effects on proliferation of normal and transformed cells in vitro" <i>Science</i> (Nov. 22, 1985) 230(4728):943-945	

Examiner's Signature	L. E. Crane <i>L. E. Crane</i>	Date Considered	09/21/2005
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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 <u>1615</u>
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

NON PATENT LITERATURE DOCUMENTS		
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<i>M.E.</i>	192	SUKUMAR and BARBACID "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> (Jan. 1990) 87:718-722
<i>M.E.</i>	193	TAKEISHI et al. "Nucleotide sequence of a functional cDNA for human thymidylate synthase" <i>Nucl. Acid Res.</i> (1985) 13(6):2035-2043
<i>M.E.</i>	194	TANNOCK "Treatment of cancer with radiation and drugs" <i>J. Clin. Oncol.</i> (Dec. 1996) 14(12):3156-3174
<i>M.E.</i>	195	TENNANT et al. "Antiviral activity and toxicity of fialuridine in the woodchuck model of hepatitis B virus infection" <i>Hepatology</i> (July 1998) 28(1):179-191
<i>M.E.</i>	196	TOLSTIKOV et al. "Synthesis and DNA duplex stabilities of oligonucleotides containing C-5-(3-methoxypropynyl)-2'-deoxyuridine residues" <i>Nucleos. Nucleot.</i> (1997) 16(3):215-225
<i>M.E.</i>	197	TOWNSEND (eds), <i>Chemistry of Nucleosides and Nucleotides</i> , Vol. 3, Plenum Press, New York, NY (1974) only Table of Contents, Bibliography, pages 529-535 and Index pp. 537-552 supplied
<i>M.E.</i>	198	TROUTNER "Chemical and physical properties of radionuclides" <i>Nucl. Med. Biol.</i> (1987) 14(3):171-176
<i>M.E.</i>	199	UBEDA and HABENER "The large subunit of the DNA replication complex C (DSEB/RF-C140) cleaved and inactivated by Caspase-3 (CPP32/YAMA) during fas-induced apoptosis" <i>J. Biol. Chem.</i> (Aug. 1, 1997) 272(31):19562-19568
<i>M.E.</i>	200	VALETTE et al. "Decomposition pathways and <i>in vitro</i> HIV inhibitory effects of isoddA pronucleotides: Toward a rational approach for intracellular delivery of nucleoside 5'-monophosphates" <i>J. Med. Chem.</i> (1996) 39:1981-1990
<i>M.E.</i>	201	van de VIJVER et al. "Amplification of the <i>neu</i> (c-erbB-2) oncogene in human mammary tumors is relatively frequent and is often accompanied by amplification of the linked c-erbA oncogene" <i>Mol. Cell. Biol.</i> (May 1987) 7(5):2019-2023
<i>M.E.</i>	202	van LAAR et al. "Comparision of 5-fluoro-2'-deoxyuridine with 5-fluorouracil and their role in the treatment of colorectal cancer" <i>European J. Cancer</i> (1998) 34(3):296-306
<i>M.E.</i>	203	VOLM et al. "Relationship of inherent resistance to doxorubicin, proliferative activity and expression of P-glycoprotein 170, and glutathione S-transferase- <i>ii</i> in human lung tumors" <i>Cancer</i> (Aug. 15, 1992) 70(4):764-769
<i>M.E.</i>	204	WAHBA and FRIEDKIN "Direct spectrophotometric evidence for the oxidation of tetrahydrofolate during the enzymatic synthesis of thymidylate" <i>J. Biol. Chem.</i> (Mar. 1961) 236(3):C11-C12
<i>M.E.</i>	205	WANG et al. "Identification and characterization of Ich-3, a member of the interleukin-1 β converting enzyme (ICE)/Ced-3 family and an upstream regulator of ICE" <i>J. Biol. Chem.</i> (Aug. 23, 1996) 271(34):20580-20587

Examiner's Signature

L. E. Crane

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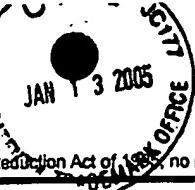
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10/048,033 - PTO-1449 #3

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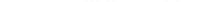
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<p>Sheet</p>		15	of	15	Attorney Docket Number	
					NB 2006.01	
					Application Number	10/048,033
					Filing Date	November 28, 2002
					First Named Inventor	H. Michael SHEPARD
					Art Unit	1623 --1615--
					Examiner Name	Not Yet Assigned

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Sheet

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Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
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U.S. PATENT DOCUMENTS

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		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
<i>He</i>	1	DE 32 29 169 A1	02-09-84	De Clercq et al.		
<i>He</i>	2	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
<i>He</i>	3	EP 0 311 108 A2	04-12-89	Stichting REGA VZW		
<i>He</i>	4	EP 0 316 592	05-24-89	Stichting REGA VZW		
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<i>He</i>	6	RO 88451	01-30-86	Antibiotics Enterprise, Iasi		X
<i>He</i>	7	WO 89/05817	06-29-89	Nucleic Acid Research Institute		
<i>He</i>	8	WO 90/03978	04-19-90	Stichting REGA VZW		
<i>He</i>	9	WO 91/17424	11-14-91	Vical, Inc.		
<i>He</i>	10	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		
<i>He</i>	11	WO 93/06120	04-01-93	University of Rochester		

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L. E. Crane

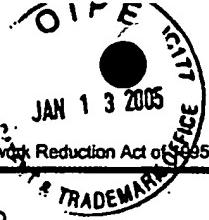
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<p>Substitute for form 1449A-PTO</p> <p>TRADEMARK</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				<p align="center">Complete if Known</p>	
Sheet	2	of	5	Application Number	10/048,033
				Filing Date	November 27, 2002
				First Named Inventor	H. Michael SHEPARD
				Art Unit	1623 1615 ---
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	NB 2006.01

U.S. PATENT DOCUMENTS

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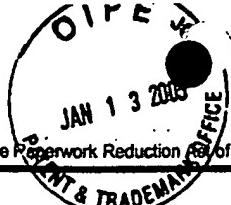
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ²
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
<i>Mel</i>	12	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
**	13	WO 94/22483	10-13-94	Kozak, Alexander		
<i>Mel</i>	14	WO 95/01806	01-19-95	Kondratyev, A.		
	15	WO 95/08556	03-30-95	Amersham International, Inc.		
<i>Mel</i>	16	WO 95/12678	05-11-95	Connors, T. et al.		
**	17	WO 95/03151	02-08-95	Springer et al.		
**	18	WO 96/07413	04-04-96	University of Georgia Research Foundation & Yale University		

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Substitute for form 1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 3 of 5

 INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
Substitute for form 1449A-PTO				Application Number	10/048,033
			Filing Date	November 27, 2002	
			First Named Inventor	H. Michael SHEPARD	
			Art Unit	1623 --1615--	
			Examiner Name	Not Yet Assigned	
Sheet	3	of	5	Attorney Docket Number	NB 2006.01

U.S. PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ²
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
JKC	19	WO 96/10030	04-04-96	Isis Pharmaceuticals, Inc.		
JKC	20	WO 96/29336	09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		
JKC	21	WO 96/33168	10-24-96	Kumiai Chemical Industry Co Ltd et al.		
JKC	22	WO 96/40088	12-19-96	Hostettler, Karl Y.		
JKC	23	WO 96/40708	12-19-96	La Jolla Pharmaceuticals, Inc.		
JKC	24	WO 96/40739	12-19-96	Terrapin Technologies, Inc.		
JKC	25	WO 97/25342	07-17-97	Terrapin Technologies, Inc.		

Examiner's Signature	L. E. Crane <i>L. E. Crane</i>	Date Considered	09/21/2005
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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet

4

of

5

Complete if Known

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			
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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
XK	26	WO 97/28179	08-07-97	Fick, James & Israel, Mark		
Yee	27	WO 97/49717	12-31-97	Balzarini et al.		
WEC	28	WO 98/49177	11-05-98	University College Cardiff Consultants Limited		
Yee	29	WO 99/06072	02-11-99	Boehringer Mannheim Corp.		
ZK	30	WO 99/20741	04-29-99	Geron Corporation		
Yee	31	WO 99/23104	05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		

Examiner's Signature

L. E. Crane

Date Considered

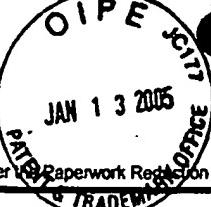
09/21/2005

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

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of

5

Complete if Known

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 =-1645=-
Examiner Name	Not Yet Assigned

Attorney Docket Number

NB 2006.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
<i>ME</i>	32	WO 99/37753	07-29-99	NewBiotics, Inc.		
<i>ME</i>	33	WO 00/18775	04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
	34	WO 00/33888	06-15-00	Dubois, V. et al.		
	35	WO 01/07088	02-01-01	NewBiotics, Inc.		
	36	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
<i>ME</i>	37	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

Examiner's Signature

L. E. Crane

Date Considered

09/21/2005

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ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18
 Stylesheet Version v18.0

P. 1 of 2

Title of Invention	METHODS FOR TREATING THERAPY-RESISTANT TUMORS
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Application Number : 10/048033 
 Confirmation Number: 2767
 First Named Applicant: H. SHEPARD
 Attorney Docket Number: NB 2006.01
 Art Unit: 1615 / 23
 Examiner: Not Yet Assigned
 Search string: (3852266 or 4247544 or 4267171 or 4542210 or 4668777 or 4816570 or 4948882 or 4963263 or 4963533 or 4975278 or 5070082 or 5077282 or 5077283 or 5085983 or 5116822 or 5116827 or 5133866 or 5137724 or 5212161 or 5212291 or 5217869 or 5233031 or 5264618 or 5300425 or 5338659 or 5430148 or 5439555 or 5457187 or 5459127 or 5516631 or 5521161 or 5527900 or 5596018 or 5616564 or 5627165 or 5645988 or 5663321 or 5733896 or 5798340 or 5968910 or 5981507 or 6057305 or 6245750 or 6339151 or 6495553 or 20010034440).pn

US Patent Documents

Note: Applicant is not required to submit a paper copy of cited US Patent Documents

init	Cite.No.	Patent No.	Date	Patentee	Kind	Class	Subclass
AA	1	3852266	1974-12-03	Kiyanagi et al.			
	2	4247544	1981-01-27	Bergstrom et al.			
	3	4267171	1981-04-12	Bergstrom et al.			
	4	4542210	1985-09-17	Sakata et al.			
	5	4668777	1987-05-26	Caruthers et al.			
	6	4816570	1989-03-28	Farquhar			
	7	4948882	1990-08-14	Ruth			
	8	4963263	1990-10-16	Kauvar			
	9	4963533	1990-10-16	de Clercq et al.			
	10	4975278	1990-12-04	Senter et al.			
	11	5070082	1991-12-03	Murdeek et al.			
	12	5077282	1991-12-03	Murdock et al.			
	13	5077283	1991-12-31	Murdock et al.			
	14	5085983	1992-02-04	Scanlon			
	15	5116822	1992-05-26	De Clercq et al.			
	16	5116827	1992-05-26	Murdeek et al.			
	17	5133866	1992-07-28	Kauvar			
	18	5137724	1992-08-11	Balzarini et al.			
	19	5212161	1993-05-18	Moriniero et al.			

Examiner Name	Date
L.E. CRAVE	09/21/2005

** Duplicate citations: see PTO-892 for citations.

10/048,033 - PTO-1449 #1

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ELECTRONIC INFORMATION DISCLOSURE STATEMENT

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Stylesheet Version v18.0

P.2/2

Title of Invention	METHODS FOR TREATING THERAPY-RESISTANT TUMORS
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Application Number: 10/048033
 Confirmation Number: 2767
 First Named Applicant: H. SHEPARD
 Attorney Docket Number: NB 2006.01
 Art Unit: 1615-1623
 Examiner: Not Yet Assigned



** 20	5212291	1993-05-18	Murdock et al.			
** 21	5217869	1993-06-08	Kauvar			
** 22	5233031	1993-08-03	Borch et al.			
** 23	5264618	1993-11-23	Felgner et al.			
** 24	5300425	1994-04-05	Kauvar			
** 25	5338659	1994-08-16	Kauvar et al.			
** 26	5430148	1995-07-04	Webber et al.			
** 27	5433955	1995-07-18	Bredehorst et al.			
** 28	5467187	1995-10-10	Gmeiner et al.			
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** 30	5516631	1996-05-14	Frisch			
** 31	5521161	1996-05-28	Malley et al.			
** 32	5527900	1996-06-18	Balzarini et al.			
** 33	5596018	1997-01-21	Baba et al.			
** 34	5616564	1997-04-01	Rapaport et al.			
** 35	5627165	1997-05-06	Glazier			
** 36	5645988	1997-07-08	Vande Woude et al.			
** 37	5663321	1997-09-02	Gmeiner et al.			
** 38	5733896	1998-03-31	Holy et al.			
** 39	5798340	1998-08-25	Bischofberger et al.			
** 40	5968910	1999-10-19	Balzarini			
** 41	5981507	1999-11-09	Josephson et al.			
** 42	6057305	2000-05-02	Holy et al.			
** 43	6246760	2001-06-12	Shepard			
** 44	6399151	2002-02-15	Shepard et al.			
** 45	6495553	2002-12-17	Shepard			

** Duplicate citations: see PTO-892 for citations.
US Published Applications

Note: Applicant is not required to submit a paper copy of cited US Published Applications

init	Cite.No	Pub. No.	Date	Applicant	Kind	Class	Subclass
88	1	2001000344401	2001-10-26	Shepard et al.			

Signature

Examiner Name L.E. CRANE	Date 09/21/2005
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** Duplicate citations: see PTO-892 for citations.

10/048,033 - PTO-1449 #1

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